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CASE REPORT

Excretion of *Ascaris lumbricoides* following reduced-intensity allogeneic hematopoietic stem cell transplantation and consecutive treatment with mebendazole

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Abstract

Here, we present the unique case of a 51-year-old German patient with multiple myeloma excreting *Ascaris lumbricoides* in his stool five weeks after allogeneic hematopoietic stem cell transplantation. Stool analysis remained negative for the presence of eggs, and there was no eosinophilia in the peripheral blood at any time around stem cell transplantation. The patient was commenced on a three-day treatment with mebendazole, which was well tolerated. No serious interactions with the concomitant post-transplant medication or negative effects on the hematopoiesis were observed, and the myeloma still is in complete remission. To our knowledge, this is the first report on excretion of *A lumbricoides* in the context of allogeneic stem cell transplantation. The case is remarkable with view to the fact that the parasite has supposedly survived all courses of myeloma treatment including autologous and allogeneic conditioning. Parasitosis with *A lumbricoides* has a worldwide prevalence of about a billion and is extremely rare in northern Europe. Possibly the patient got infected during a trip to Egypt years before multiple myeloma was diagnosed.

KEYWORDS

Ascaris lumbricoides, hematopoietic stem cell transplantation, mebendazole, multiple myeloma, mycophenolic acid, sirolimus

1 | CASE REPORT

Helminth infections are known to be a worldwide problem with high prevalence, especially in less developed countries.[1,2] Nevertheless, data about parasitic diseases in the context of allogeneic hematopoietic stem cell transplantation (HSCT) are very limited. At our transplant center, we observed a case of intestinal infection with *Ascaris lumbricoides* in a patient who underwent HSCT for treatment of multiple myeloma. Written informed consent was obtained from the patient for publication of this case report.

A 51-year-old German male patient was diagnosed with multiple myeloma (subtype IgG lambda) in stage II B according to *Salmon and Durie* and stage III according to *Revised International Staging System* (R-ISS), respectively.[3] At that time, β2-microglobulin in the serum was 43.2 mg/L and creatinine in the serum was 8.9 mg/dL. Hemodialysis had to be performed immediately because of acute renal failure. In addition, lytic lesions were found in thoracic spine, sternum, and

pelvis. Cytogenetic and molecular genetic analyses of malignant cells showed trisomy 3, IGH-FGFR3 rearrangement, TP53 deletion, and 13q14 deletion. Several years before, the patient was diagnosed with highly malignant B-cell lymphoma. However, he was in ongoing complete remission (CR) after having received several courses of polychemotherapy. Other relevant diagnoses could not be found.

Subsequently, three courses of induction chemotherapy according to the "PAD combination therapy" regimen (containing bortezomib, doxorubicin, and dexamethasone[4]) were applied followed by one course of high-dose melphalan with autologous stem cell support. Subsequent staging showed CR of multiple myeloma, and the patient was sent to our transplant center. We offered him allogeneic HSCT for high-risk myeloma as a possibility to definite cure. His brother was identified as a possible 10/10 HLA-matched donor. After written informed consent, he received peripheral blood stem cell graft after reduced-intensity conditioning therapy with fludarabine and treosulfan (days −4 to −2). Irradiation or anti-thymocyte globulins were not part of the conditioning therapy. Sirolimus and mycophenolate mofetil (MMF) were used as immunosuppressive therapy afterward. Engraftment of neutrophils was documented on day +12 after application of granulocyte colony-stimulating factor and engraftment of platelets on day +11.

During transplantation, the patient was suffering from diarrhea. Reverse transcriptase-polymerase chain reaction of stool specimens revealed *Norovirus* infection. Diarrheal symptoms were presumed to be related to *Norovirus* infection, and no further tests were performed to identify other causes of infectious diarrhea. In the following days, diarrhea ceased and the patient was discharged from hospital. *Norovirus* was tested negative several times afterward.

The patient showed up for post-transplant follow-up in our outpatient transplant center 35 days after HSCT. He reported an unusual observation after defecation, revealing a white longish structure, which he brought with him (Figure 1). We assumed the object to be a dead worm. The parasite was sent to the *Institute for Hygiene and Microbiology at the University of Würzburg*, where it was confirmed to be *A lumbricoides* by visual inspection.

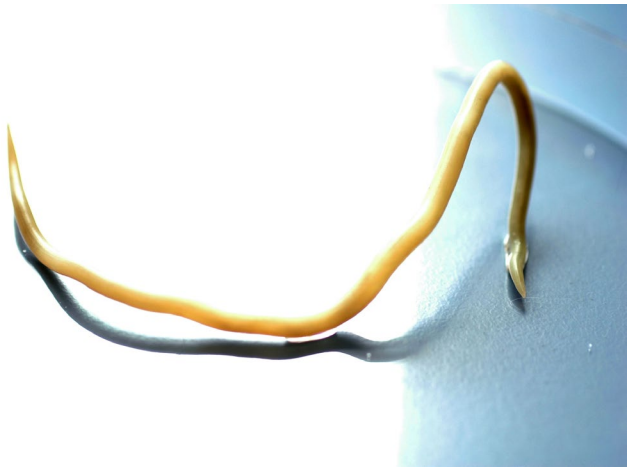

FIGURE 1 *Ascaris lumbricoides*, found after defecation in a 51-y-old male patient who underwent allogeneic hematopoietic stem cell transplantation for his multiple myeloma

At the time of the excretion of the parasite, the patient was feeling well and had no signs of infection, diarrhea, or malabsorption. Helminth eggs were not seen on microscopic examination of sodium acetate/acetic acid/formalin-fixed stool samples. No evidence of graft-versus-host disease could be found. The patient did not undergo further imaging or endoscopic examination. No elevation of eosinophils in peripheral blood was seen at any time around allogeneic HSCT. Serum analysis of liposoluble vitamins showed normal levels. At the time of excretion, the patient's medication consisted of sirolimus, MMF, prednisolone, acyclovir, fluconazole, cotrimoxazole, pantoprazole, potassium, and vitamin B complex.

There is no suggestion how patients with *ascariasis* in this special case of allogeneic HSCT or other reasons for immunodeficiency should be treated—or should be treated at all. Even no information could be found about drug interactions with post-transplant prophylaxis. Although further evidence for invasive *ascariasis* could not be found, we decided to treat the patient the way it would have been suggested in the absence of allogeneic HSCT. The patient was given mebendazole 100 mg twice a day for 3 days (Figure 2). Adverse reactions after application of mebendazole could not be found, and relevant drug interactions were not observed. After treatment with mebendazole, new symptoms of helminthiasis or a second excretion of a worm was never observed. The patient never showed any relevant infectious complications after the episode of *Ascariasis*, and no intestinal problems had to be noted.

2 | DISCUSSION

It is well known that many infections with *A lumbricoides* stay inapparent.[5,6] After ingestion of worm eggs, that is, by consumption of salad that was contaminated during manuring, larvae emerge in the small intestine and migrate through the venous system to the liver and the lung. In the latter, they are expectorated through the trachea and swallowed again leading them back to the small intestine, where they grow to adult worms.[7,8] Complications of migrating larvae of *A lumbricoides* include eosinophilic pulmonary infiltrates with respiratory failure (Loeffler's syndrome) and obstruction of the intestine or the bile duct.[9-11] *Ascariasis* often causes blood eosinophilia.[12,13] In the literature, only few similar cases can be found. However, one case of excretion of *A lumbricoides* has been described in a patient receiving high-dose chemotherapy and total body irradiation in preparation for autologous HSCT. The patient was treated the same way as in our case and showed no further symptoms of helminth infection.[14]

The origin of the infection in the patient reported here is not completely clear. Years before the allogeneic HSCT mentioned above, he used to travel around the world and visited Egypt, among other countries. In between, he never showed any symptoms of parasitosis. Furthermore, his last journey to foreign countries was long before multiple myeloma was diagnosed and the patient's family never showed any symptoms of helminth infection. By now,

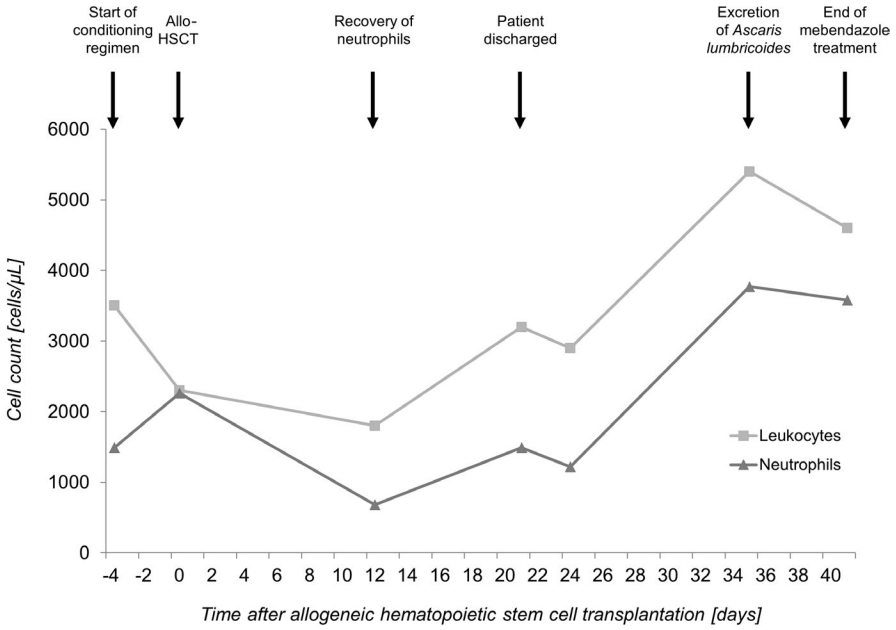

FIGURE 2 Schematic diagram showing absolute leukocyte (normal range: 4.0-10. × 10^3/µL) and neutrophil (normal range: 1.5-7.0 × 10^3/µL) counts and clinical course of the patient around allogeneic hematopoietic stem cell transplantation (allo-HSCT)

the patient is still in ongoing CR of both hematologic diseases mentioned above.

The most remarkable aspect in this case is obviously the fact that *A lumbricoides* appeared 35 days after starting toxic chemotherapy. With a new infection being unlikely based on the most recent history, it can only be assumed that the parasite deceased just before being excreted, implicating survival under autologous and allogeneic conditioning including exposition to fludarabine and treosulfan. Fludarabine, a purine analogue, and treosulfan, an alkylating agent, are assumed to interfere with helminths' cell cycle and with human bone marrow cells.[15] The immunosuppressive agents sirolimus and MMF also might have had a strong effect on the worm's cell cycle.[16-20]

3 | CONCLUSION

Although helminth infections are a common problem all over the world, *ascariasis* in the context of allogeneic HSCT was never reported in the literature before. We observed a unique case of excretion of *A lumbricoides* following autologous HSCT and consecutive reduced-intensity allogeneic HSCT in a patient with multiple myeloma. It is still not known what made the parasite to decease an association with toxic drug effects of either conditioning chemotherapy or immunosuppressive agents being the most likely. Finally, it remains open what has caused the worm's death. Nonetheless, the uniqueness of the present case is certainly the appearance of the usually inapparent.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

Verena Luber and Mathias Lutz made substantial contributions to the conception of the work, analyzed data, and wrote the manuscript. Marianne Abele-Horn made substantial contributions to the conception of the work and performed microbiological analyses. Hermann Einsele and Götz Ulrich Grigoleit made substantial contributions to the conception of the work and analyzed data. Stephan Mielke made substantial contributions to the conception of the work, analyzed data, and wrote the manuscript. All authors critically revised the manuscript for important intellectual content and approved the final manuscript to be published.

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